THERAPEUTICS

UNDER THE CHARGE OF

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Influence of Some Drugs Used in Treatment of Gout.—DENIS (*Jour. Pharm. and Exper. Ther.*, 1915, vii, 601) says that sodium benzoate, atophan and the salicylates including aspirin, when given in sufficiently large amounts cause an increased elimination of uric acid from the blood. This effect lends some support to the view that the good effects produced by the drugs at present considered by clinicians as most efficient in the treatment of gout may in part at least be due to a power possessed by them of producing a lowered kidney threshold for certain specific substances. Atophan and the salicylates possess this power in a marked degree. Benzoic acid when administered in large doses (8 gm. per day) increases the uric acid excretion in the urine and decreases the uric acid content of the blood. Cinnamic acid in the comparatively small doses used (4 to 6 gm. per day) have little, if any, effect. Quinic acid and colchicum have also no effect on the uric acid elimination. The same is true of para-oxybenzoic acid which shows none of the power possessed by its homologue, salicylic acid, of producing a lowered kidney threshold for uric acid. None of these drugs produce any change in the non-protein nitrogen content of the blood. Benzoic acid, aspirin and atophan were found to have no effect on the creatin content of the blood.

The Uric Acid Solvent Power of Urine After Administration of Piperazin, Lysidin, Lithium Carbonate and other Alkalies.—HASKINS (*Arch. Int. Med.*, 1916, xvii, 405) found that piperazin can cause the urine to dissolve more uric acid than it would without the drug, and this effect is most marked if sodium citrate or bicarbonate be also given and if diuresis be avoided. Lysidin can act as a uric acid solvent but is not a practical therapeutic agent because of the large doses required. Lithium carbonate is a uric solvent if large enough doses are used, but is unsafe and possesses no advantage over sodium citrate or bicarbonate. Sodium citrate and bicarbonate are reliable and satisfactory uric acid dissolving agents when given in such dosage as to keep the urine alkaline.

The Standardization of Digitalis and the Potency of American-grown Digitalis.—ROWNTREE and MACHT (*Jour. Amer. Med. Assn.*, 1916, lxvi, 870) relate their investigations which strikingly emphasize the need of standardization of digitalis. Variations in lethal dose from 6.6 to 19 c.c. per kilogram weight, approximately 300 per cent., were found in the infusions prepared from digitalis leaves of different sources. This difference is greater than should be tolerated by the profession. The different leaves tested by the authors were all obtained from very reliable sources, and in all probability greater variations exist in leaves purchased in the open market. The authors emphasize that standardization reveals the strength of the digitalis preparation and permits of graded dosage—more or less—according to the potency of the preparation. The physician's duty to his patient does not end with the prescribing of digitalis. Plainly it is incumbent on him to secure digitalis effects if the case is a suitable one. This is more likely to be accomplished if the potency of the preparation is known. It is especially interesting at this time to find that certain American-grown digitalis leaves yielded a product superior in potency to those made from English and German leaves.

Remarks on Bacillus Welchii in the Stools of Pellagrins.—HOLMES (*Arch. Int. Med.*, 1916, xvii, 453) says that B. welchii has been found with marked regularity in the stools of pellagrins in numbers greater than normal. These pellagrins were on a dietary composed principally of vegetable foods high in carbohydrate content. The diet was extremely low in protein and especially in protein of animal origin. Holmes notes the facts that diarrhea is one of the most constant symptoms of the disease known as pellagra and that B. welchii has been found to produce severe diarrhea in children and adults in the presence of a high carbohydrate diet. Furthermore, diarrhea caused by B. welchii can be cured by a protein and buttermilk diet. The author calls attention to the fact that Goldberger has prevented pellagra by the addition of proteins and buttermilk in the diet, and has experimentally caused pellagra by means of a pure carbohydrate diet. He believes that the above facts by no means prove that B. welchii is the direct or sole cause of pellagra but believes their coincidence is sufficiently significant to justify further observation.

Venesection as a Therapeutic Measure.—LAWRENCE (*Bost. Med. and Surg. Jour.*, 1916, clxxiv, 203) says that venesection performed under proper indications, is not a dangerous measure, especially since the "dose" can be accurately controlled. In the presence of dilatation of the heart, renal toxemia, hypertension or a combination of these conditions, it may be expected to act more promptly and more surely than drugs. It lowers blood-pressure and at the same time produces a more efficient circulation when performed in cases of hypertension, but does not, in therapeutic "doses" lower normal arterial tension. Venesection should never be performed in the absence of definite indications, but should not be withheld until the hope of success from any measure is gone. The amount of blood to be withdrawn is to be decided by the point at which relief is to be obtained. The error is generally on the side of removing too small an amount. Repeated blood-letting, when indicated, does not seem to have any ill effects upon the composition of the blood.

Corpus Luteum Extract in the Nausea of Pregnancy.—HIRST (*Jour. Amer. Med. Assn.*, 1916, lxvi, 645) reports encouraging results with the hypodermic administration of corpus luteum extract for the treatment of nausea occurring in pregnancy. He bases this treatment on the presumption that there is more than a coincidence between the formation and disappearance of the corpus luteum of pregnancy and the cessation of the nausea. Only five cases are reported, four of which were successfully treated. Hirst makes this preliminary report in the hope that this treatment may be tried by others in order to determine whether or not it is of value.

Pellagra—Causation and a Method of Prevention.—GOLDBERGER (*Jour. Amer. Med. Assn.*, 1916, lxvi, 471), in a summary of his observations made in three institutions where pellagra was endemic, states that a diet containing a liberal amount of fresh animal and leguminous protein foods, without other alteration in the hygienic and sanitary conditions, successfully prevented the annual recurrence of the disease in practically 100 per cent. of the cases. Of the 209 cases of pellagra observed at the two orphanages during the spring and summer of 1914, not less than 172 completed at least the anniversary date of their attack under observation. In only one of these 172 cases, following the change in diet, was there recognized evidence of a recurrence, although on the basis of experience elsewhere, from 99 to 130 might reasonably have been expected. Nor was any new case observed among the non-pellagrin residents, 168 of whom completed not less than one year under observation. Of the group of pellagrins on the modified diet at the insane asylum, 72 remained continuously under observation up to October 1, 1915, or at least until after the anniversary date of their attack of 1914. Not one of this group has presented recognizable evidence of a recurrence, although, of a group of thirty-two controls, fifteen have had recurrences. Pellagra may, therefore, be prevented by an appropriate diet without any alteration in the environment, hygienic or sanitary, including the water supply. At an isolated convict camp, previously free from pellagra, with an average population of from seventy to eighty white males, eleven volunteers were segregated and, after a preliminary observation period of two and a half months, placed on an abundant but one-sided, chiefly carbohydrate (wheat, corn, rice) diet, from which fresh animal proteins and legumes were excluded. At least six of these volunteers developed pellagra. This result would appear to have been brought about by the diet on which they subsisted. A definite conclusion as to the intimate mechanism involved in bringing about or in preventing the disease by diet cannot be drawn from the available data. For the practical purposes of preventive medicine it would seem to be of fundamental importance to recognize that the pellagra-producing dietary "fault" is capable of correction or prevention by including in the diet suitable proportions of the fresh animal and leguminous protein foods.

The Intraspinal Administration of Mercurialized Serum.—HUNT (*Jour. Am. Med. Assn.*, 1916, lxvi, 404) reports a series of 45 cases of which 40 were given intraspinal injections of mercuric chlorid, and 5 were given sublamin injections. These patients were at the same time given intramuscular injections of mercuric salicylate every week, and in the very early ones intravenous injections of salvarsan. The cases treated comprised cases of tabes, general paresis, cerebrospinal syphilis, taboparesis, clinical tabes (tabes with a negative serology) and syphilitic hemiplegia. These patients were observed over a period of six months and Hunt believes that the number of cases is too small and the period of observation too short to draw any definite conclusion. The author found that the reaction from mercuric chlorid or sublamin in no way differed from the reaction which followed the administration of salvarsan. The sublamin did not seem to give the same reduction in the cell count or clinical improvement as did the mercuric chlorid. No ill results followed these injections. The three deaths could be easily accounted for, as the patients were practically moribund at the time of the treatment, and were given the injections as a last resort. The patients with tabes and cerebrospinal syphilis were helped more than any others. The ten patients with general paresis treated showed less improvement than almost any of the others. One-half of them showed no change and two became worse. Such improvement as did occur was evident in the feelings of the patient, in the sphincter control, in the pains, in the gait, and in the serology. There was no improvement in the reflexes. Such intraspinal treatment can be given only at intervals of two weeks, because a cell count does not fall sooner. The reaction obtained was one in which the cell count was first greatly increased and then diminished. The cell count and the globulin yielded much sooner than did the Wassermann.

The Treatment of Central Nervous System Syphilis.—Walker (*Boston Med. and Surg. Jour.*, 1916, clxxiv, 195) summarizes the treatment and results in the first 40 cases of central nervous system syphilis at the Peter Bent Brigham Hospital. This group includes cases of tabes, general paresis, cerebrospinal syphilis and syphilitic meningitis; cases of purely cerebral syphilis are excluded. In the treatment of parasyphilis three methods were employed: one, salvarsan, intravenously alone; another, the Swift-Ellis method; and a third, salvarsanized serum alone intraspinally. Walker used large doses of salvarsan intravenously for those cases treated with salvarsan alone; in those treated with serum intraspinally 20 to 25 c.c. of undiluted serum were used. It was found that cases of syphilis of the central nervous system with only a positive blood react well to salvarsan; those with a positive blood and spinal fluid may react well to salvarsan alone, but they do much better when intraspinal serum is used in conjunction with salvarsan, and some who do not react to salvarsan alone do react well to the combined method. One may obtain improvement in general paresis with the combined treatment. Cases of syphilitic meningitis may clear up with salvarsan alone but the combined treatment is the quickest. Cases of central nervous system syphilis with a negative blood and positive spinal fluid findings react readily to salvarsanized serum intraspinally alone, even when salvarsan intravenously has failed. The spinal fluid of the cases treated with salvarsan has become negative in two cases, whereas the spinal fluid of seven cases treated with the serum alone has become negative. The author feels that salvarsanized serum is a great asset in the treatment of syphilis of the central nervous system, and in the general run of cases he thinks the Swift-Ellis method is of great value and that this method in conjunction with mercury given intramuscularly is the best treatment of syphilis of the central nervous system at the present time. Marked improvement always follows such treatment.

The Comparative Pharmacological Action of Ethylhydrocuprein (Aptochin) and Quinin.—Smith and Fantus (*Jour. of Pharm. and Exper. Ther.*, 1916, viii, 53) call attention to some facts regarding optochin which are important because of the increasing use of the remedy for the treatment of pneumonia. Optochin is an alkaloid derived from cuprea bark and in its chemical structure is closely related to quinin. While quinin chemically is methoxycinchonin, optochin is a hydroxycinchonin. Morgenroth, in 1911, reported that he was able to protect over 90 per cent. of animals against artificial pneumococcus infection by injections of optochin. His work has been confirmed by others and particularly of late many favorable reports have been made regarding its therapeutic use in lobar pneumonia. The authors found that the pharmacological action of optochin is qualitatively like that of quinin, but differs in degree. Optochin is more toxic than quinin. In view of its considerable degree of toxicity, the authors urge caution in the clinical use of optochin, especially in its intravenous administration. They found that when administered intravenously it lowers the blood-pressure somewhat less than quinin although it depresses the heart more. The peripheral vasoconstriction probably counteracts partly the effects of cardiac depression. Optochin was not so efficient an antipyretic as quinin in experimental fever of animals. Optochin has been advocated for local use in eye infections, particularly those due to the pneumococcus, but the authors found that even a 2 per cent. solution was highly irritant to the conjunctiva.

The Treatment of Typhoid Fever by Intravenous Injections of Polyvalent Sensitized Vaccine Sediment.—Gay and Chickering (*Arch. Int. Med.*, 1916, xvii, 303) report a series of 53 cases of typhoid fever, in which the diagnosis was absolutely certain both on clinical and on laboratory grounds, treated by intravenous injections of a sensitized polyvalent typhoid vaccine. These patients were cared for under varying conditions in private houses and hospitals. The mortality in these cases has been precisely what one would expect under the best hospital conditions (9 per cent.), which the authors regard as suggesting that, under uniform conditions, with their method of treatment the mortality would have been less than the average. The mortality has been composed, to a large extent, of what may be termed "accidents" of typhoid, namely 60 per cent. of deaths by hemorrhage or perforation. Their method of treatment has consisted in the intravenous injection of $\frac{1}{50}$ to $\frac{1}{25}$ mg. (150 to 300 million bacteria) of a sensitized, polyvalent, killed typhoid vaccine sediment prepared after the method of Gay and Claypole. This injection gives rise to a series of symptoms characterized particularly by a chill, rise and fall of temperature, and leukopenia followed by hyperleukocytosis. The fall of temperature with its attendant hyperleukocytosis leaves the patient at least temporarily benefited, and the benefit and normal temperature may be permanent. Thus in 66 per cent. of the cases a distinct benefit was obtained, as shown by lowered temperature, disappearance or amelioration of subjective symptoms and an apparently accelerated recovery. In 41.5 per cent. of this 66 per cent. the recovery was of an abortive form with a critical fall of temperature and a permanent normal temperature established within a few days. This permanent normal temperature was reached on an average seven days after beginning treatment in these cases. There remains, however, 34 per cent. of cases which are classified as relatively unaffected. They regard this classification as underestimating the beneficial results for reasons given. In none of the cases did the use of the vaccine have any apparent harmful effect on the case, although in four, in which too large a dose was used, the symptoms were somewhat alarming. A series of subcutaneous injections following the intravenous treatment apparently aids in preventing relapses. The authors regard the mechanism of benefit and cure in these cases which were affected by the treatment as due to a combination of specific hyperleukocytosis and the presence of antibodies in the patient's blood. The injection of vaccine could be shown in a number of cases to be followed by the disappearance or diminution of bacteremia and usually also by an increase in the Widal. In those cases which did best the Widal was originally high and those cases which showed the least effect had the low Widals. The cases judged as "mild" before treatment began did better on the whole than those regarded as "severe." There were, however, a number of severe cases which showed abrupt recovery or benefit. On the hypothesis that successful results are due to the strength of the antibodies already established in the patient, Gay and Chickering ventured in severe cases with low antibody content, to combine with the vaccine treatment the intravenous injection of considerable amounts of typhoid immune serum from goats. These cases, although few in number, suggest that this type of treatment with further elaboration might increase the percentage of favorable results. They regard the use of sensitized vaccine as being better for intravenous injection than plain typhoid vaccine or less specific methods of treatment that have been suggested by other authors, owing to the fact that sensitized typhoid vaccine produces a specific form of hyperleukocytosis of maximum degree (Gay and Claypole), and may also be shown to be followed by an increase in active immunity of the patient against the disease.

The Intravenous Administration of Mercury in Syphilis.—Shaw (*Med. Record*, 1916, lxxxix, 823) reports 16 cases of syphilis treated by intravenous injections of mercuric chlorid with good results. The dose used was ⅛ to ⅙ of a grain to a patient of 140 to 150 pounds body weight, every five to seven days. Shaw says that this method is quick, safe and certain; the dose can be very accurately measured and the administration is free from pain. The therapeutic effects are just as quick, in many cases more certain and more permanent than those following salvarsan and neosalvarsan. This method is recommended also because of its availability and cheapness. The administration is attended with no untoward results except for a low grade of phlebitis which may produce obliteration of the vein used and which is in proportion to the concentration of the solution used.